

Report Title: Primary Skin Irritation Study in Albino Rabbits

Test Type: Skin Irritation

Conducting Laboratory and Location: International Research and Development Corporation

Test Substance(s): T-7121 – 2% Placebo shampoo at pH 4.5

Species: Rabbit

of Animals: 3 male New Zealand White rabbits

Test Conditions: 3 male New Zealand White rabbits exposed to two patches on the back with 0.4 ml applied as a 10% (w/w) solution in distilled water for 24 hr. One patch was applied to intact skin and the other to abraded skin. Test sites were graded at 24 and 72 hr.

Results: NOT a primary skin irritant. Score: 4.0

Study #: 191-082; see related studies 191-080 and 191-081

Report Date: 12/5/77

Accession #: 19199

International Research and Development Corporation

SPONSOR: Procter and Gamble Company
TEST MATERIAL: T 7121
STUDY NUMBER: 191-082 1397
SUBJECT: Primary Skin Irritation Study
in Albino Rabbits.



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Director of Acute Toxicology
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Approved by: D. Clifford Jessup, Ph.D.
Associate Director of Research

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H. A. DERNER

Date: December 5, 1977

International Research and Development Corporation

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I. SYNOPSIS

Not a primary skin irritant.

Primary Irritation Score = 4.0.

II. TEST MATERIAL

The test material was received from Procter and Gamble Company, Cincinnati, Ohio on August 4, 1977. It was identified as "T 7121" and was received as a slightly yellow viscous liquid.

III. METHOD

Three male New Zealand White rabbits (obtained from Kuiper's Rabbit Ranch, Gary, Indiana) were used for this study. The rabbits weighed from 2046 to 2241 grams at the beginning of the study. They were individually housed in metal metabolism cages in temperature and humidity controlled quarters. They were maintained in accordance with the recommendations contained in H.E.W. Publication No. 74-23 (N.I.H.) entitled "Guide for the Care and Use of Laboratory Animals" and were conditioned for 6 days prior to study initiation. Water and Purina Rabbit Chow were available ad libitum.

The hair was removed from the back of each rabbit (20-30% of the body surface) with an electric clipper. The back of each rabbit had one abraded and one intact site. A clipper head was used for the abrading. The abrading was not sufficiently deep to cause bleeding.

A volume of 0.4 milliliter of the test material was applied, as a 10% (w/w) solution in distilled water, to each of two 38 x 38 mm Parke-Davis Rendi-Bandages with a 20 x 20 felt pad which were then placed on the two sites on the backs of each of the rabbits. The patches were secured in place with several wrappings of 75 mm Elastoplast tape and collars were placed on each rabbit. Following the 24 hour application period, the collars and patches were removed and any remaining test material was removed with a damp cloth.

Thirty minutes following the removal of the wrappings, the sites were examined for skin irritation in accordance with the scale on page 4. These examinations were repeated at 72 hours. (See attached protocol for specific experimental design used.)

Value *

Erythema and Eschar Formation:

No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4

Edema Formation:

No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raising approximately 1.0 mm)	3
Severe edema (raised more than 1.0 mm extending beyond the area of exposure)	4

IV. RESULTS

The table below presents the grade of effect with time. Table 1 presents the individual rabbit scores and the computed primary irritation score of 4.0.

Based upon the results obtained, T 7121 would not be considered a primary skin irritant.

The test material would be further classified, based upon the scores obtained, as being moderately irritating to the skin when evaluated using the method described in the protocol.

Number of Animals Exhibiting Signs with Scoring "Value"

Observations	Value	<u>Intact Skin</u>		<u>Abraded Skin</u>	
		<u>Hours</u>		<u>Hours</u>	
		<u>24</u>	<u>72</u>	<u>24</u>	<u>72</u>
Erythema,	0				
Eschar	1		1/3	1/3	1/3
Formation	2	3/3	2/3	2/3	2/3
	3				
	4				
Edema	0				
Formation	1		1/3	1/3	1/3
	2	2/3	1/3	1/3	1/3
	3	1/3	1/3	1/3	1/3
	4				

Number of Animals Exhibiting "Other" Signs

Blanching	3/3	2/3	2/3	2/3
Coriaceousness	0/3	2/3	0/3	2/3

T 7121:

Individual Rabbit Scores and Score Calculation

1.

Intact Skin

Animal No./Sex	Erythema					Edema				
	Observation Period (Hours)					Observation Period (Hours)				
	24	72				24	72			
29907, Male	2.0 ^b	2.5 ^{bc}				2.0	2.0			
29927, Male	2.0 ^b	2.5 ^{bc}				3.0	3.0			
29937, Male	2.0 ^b	1.5				2.0	1.0			
Total	6.0	6.5				7.0	6.0			
Average (Value)	2.0	2.2				2.3	2.0			

Abraded Skin

Animal No./Sex	Erythema					Edema				
	Observation Period (Hours)					Observation Period (Hours)				
	24	72				24	72			
29907, Male	2.0 ^b	2.5 ^{bc}				2.0	2.0			
29927, Male	2.0 ^b	2.5 ^{bc}				3.0	3.0			
29937, Male	1.5	0.5				1.5	0.5			
Total	5.5	5.5				6.5	5.5			
Average (Value)	1.8	1.8				2.2	1.8			

Calculation for Primary Skin Irritation Score (Score = sum of the values {averages} divided by the number of observation periods used in evaluating the Primary Irritation Score times 2):
 $16.1 \div 4 = 4.0$

b - blanching

c - coriaceousness

INTERNATIONAL RESEARCH AND DEVELOPMENT CORPORATION

Lab Project No. 191-082 Sheet 1 Date 8/5/77 Authorized by *J. Jessup* Dr. Jessup

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<u>Compound</u>	<u>Identification Number</u>	<u>IRDC No.</u>
T-7121		A-327

TITLE: ACUTE TOXICITY STUDIES IN RATS AND RABBITS

Conduct in accordance with the attached protocol.

Primary Skin Irritation - Rabbit Closed Patch

Date: /

Issue #2

Purpose: To determine relative levels of primary skin irritation.

Animals: Rabbits, three New Zealand albino of either sex, weighing greater than 2 kg and showing no signs of molting.

Dosage Levels: Four-tenths (0.4) milliliter of a concentration based on previous experience or on the basis of preliminary trials.

Procedure: Before treatment, clip the rabbit backs with an Oster small animal clipper. One test site on each animal is left intact and one test site is abraded with the clipper head so as to penetrate the horny layer of the epidermis, but without causing bleeding.

Apply 0.4 ml of the appropriate concentration of test material to a 38 x 38 mm Parke-Davis Read-Bandage with a 20 x 20 mm felt pad. Place coverlets on both the intact and abraded site on each animal. Secure the patches with several wrappings of 75 mm Elastoplast tape around the animals' trunk. Place the animals in a Newmann(1) harness to prevent their removing the wrapping. After 24 hours, remove the harness and patches. Remove any test material remaining on the patch sites with a damp cloth. Thirty minutes after removal of the patches, evaluate the reactions on the basis of the table below. Evaluate again after 72 hours. Record all skin reactions not covered by the scoring table.

Scoring: Evaluation of Skin Reactions

(1) Erythema and Eschar Formation

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Highest possible erythema score	4

(2) Edema Formation

No Edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4
Highest possible edema score	4

(1) Newmann, E. A. (1963) Lab. Animal Care, 13, 207-210.

Report:

The average of all scores (3 animals, 24 and 72 hours, abraded and intact) for erythema readings. The average of all scores for edema readings. The sum of the two averages is the Primary Irritation Index. Descriptive words are correlated with values of the Primary Irritation Index, as follows:

0 - 2 = Mild

2 - 5 = Moderately irritating

5 - 6 = Moderately to severely irritating

6 - 8 = Severely irritating

File the final report within 3 weeks of completing the experimental work. -

Principal Investigator: M. J. Winrow

Date: 7/28/77